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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,430	10/03/2003	William J. Wechter	3829.01-1	1619

7590 11/19/2004

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EXAMINER	
DENTZ, BERNARD I	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,430	WECHTER ET AL.	
	Examiner	Art Unit	
	Bernard Dentz	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-9-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7, 9, 10, 11 and 15-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Zavitz et al, Published US Patent Application which was filed 6-28-2002. It discloses the C1-C6 alkyl esters of R-NSAIDS as useful for treating a patient with an aids infection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4,6,7,9,10,11 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter el al, Cancer Research, vol. 60. p. 2203-2208 (2000) in view of Zavitz et al. The former discloses that R-flurbiprofen an enantiomer of a racemic NSAID does not inhibit either cyclo-oxygenase-1 or cyclo-oxygenase-2, and in the TRAMP mouse reduces the incidence of cancer in the prostate and in metastatic sites. Applicant's claims include alkyl esters of 3-6 carbons. Zavitz in teaching an equivalence of the acid and C1-C6 alkyl esters in treating aids provides the motivation to convert the

free R-NSAID acid of Wechter et al to the above esters to provide pharmaceutically useful, in particular, anti-cancer compounds.

Claims 1-6 and 10-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter et al in view of Manfredini et al, J. of Med. Chem. article, cited by applicants. The former discloses the utility of R-NSAIDS. The latter discloses the benefits of converting a known NSAID, i.e. diclofenamic acid, to the ascorbate thereof. It improves the entry into the brain. Therefore it would have been obvious for the ordinary worker in the art to esterify the R-NSAID of Wechter et al with ascorbic acid.

Claims 1-6 and 10-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zavitz et al in view of Manfredini et al. The former disclose the benefit of using the free acid as well as lower alkyl esters of NSAIDS in the R-form in the treatment of AIDS. Because of the disclosure of Manfredini et al concerning the pharmaceutical utility of using the ascorbates of certain drugs including an NSAID, the ascorbates of the R-NSAIDS of Zavitz would have been obvious to one of ordinary skill in the art.

Claims 1-11 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zavitz et al, supra in view of Alper, EP 305089. The former is used to show the desireability of using R-esters of NSAIDS in treating aids. Alper discloses a method or making R-esters of NSAIDS. See first par. of p.2 and first complete par. of p. 3, the latter of which states that a preferred embodiment is to use derivatives of styrene, examples of which are p-isopropylstyrene and p-isobutylstyrene or 2-vinyl-6-methoxy-naphthalene ; the latter two compounds are precursors of ibuprofen and naproxen both of which are pharmaceutically important molecules.

Further see fourth par. of p. 3 where it is recited that monohydric or polyhydric alcohols which may be represented by R_2CHOH where R is independently H, alkyl aryl or hydroxyalkyl. All the monohydric alcohols of 3-6 C atoms are specifically recited as well as 1,4-butanediol. Thus a reference teaching the specific desireability of the R-esters of NSAIDS and a reference teaching the desireability of and how to make optically active esters of NSAIDS are cited. One of ordinary skill in the art would be motivated to make R-NSAID esters of 3-6 C atoms containing extra OH groups in view of the teaching of Alper when combined with Zavitz et al for use as an active ingredient in pharmaceuticals.

Claims 1-11 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter et al, supra in view of Zavitz et al and Alper. The first 2 are used to show the desireability of using R-esters of NSAIDS. Alper shows how to make them and further as explained above also includes the optically active esters of NSAIDS with polyhydric alcohols.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification doesn't recite the process

described in said claim. With ascorbic acid, applicants must protect the primary OH group, then protect the vicinal OH groups, then deprotect the primary OH group, then react the primary OH group with an activated form of the R-NSAID and then remove said protecting groups. See Ex. 1.

The third page of Manfredini et al, J. of Med. Chem. article is not in the record. Please send it in.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard Dentz whose telephone number is 571-272-0683. The examiner can normally be reached on Mon-Fri from 8 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Dentz

10-29-2004

B Dentz

BERNARD DENTZ
PRIMARY EXAMINER
ART UNIT 1625